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(54) **Imaging system for detecting diseased tissue using native fluorescence in the gastrointestinal and respiratory tract**

Bildaufnahmesystem zur Erfassung von krankem Gewebe mit nativer Fluoreszenz in Verdauungs- und Atemwegen

Système d'imagerie pour détecter de tissus maligne par la fluorescence à l'état naturel dans les voies gastro-intestinales et respiratoires

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**EP-A- 0 512 965**                      **WO-A-95/26673**

- **PATENT ABSTRACTS OF JAPAN** vol. 012, no. 494 (P-805), 23 December 1988 & JP 63 205545 A (JAPAN SPECTROSCOPIC CO), 25 August 1988,

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**Description**Field of the Invention

5 [0001] The present invention relates to cancer detection systems, and in particular to cancer detection systems that measure the native fluorescence response of normal, precancerous and cancerous tissue.

Background of the Invention

10 [0002] One of the leading causes of death among humans is cancer. Despite the high mortality rates, many cancers can be cured if detected and treated early. To that end, considerable effort has been devoted to the design and development of screening systems that aid the physician in the detection of the presence of early stage cancerous or precancerous tissue.

15 [0003] One of the more recent methods for detection and treatment of cancers in internal body cavities is fluorescence imaging. This imaging mode provides different information than the conventionally used reflectance imaging mode. In both imaging modes, the physician inserts an endoscope or fiber optic bundle into the body cavity which conducts illumination into the cavity from a light source. In reflectance imaging, the light source is typically white light whereas in fluorescence, a specific excitation wavelength(s) is used. The reflectance or fluorescence image is captured by the imaging fiber bundle of the endoscope and viewed by the physician through the ocular of the endoscope. Alternatively, 20 a camera can be attached to the ocular so that the image can be displayed on a monitor.

[0004] In prior art fluorescence imaging systems, a physician typically prepares a patient by administering a photosensitive drug that binds to cancerous tissue. The photosensitive drugs cause the cancerous tissue to contrast with the surrounding tissue, thereby allowing the physician to visually detect the presence of cancer. The problem with the use of photosensitive drugs to detect cancer is that most drugs have significant side effects. The most serious side effect is that the patients become hyper sun sensitive while the drugs are active. Therefore, patients who receive these drugs must be kept in darkened rooms for several days after the administration of the drugs. This method of cancer detection is therefore not suited for screening applications where it is desired to test as many patients as possible in the least amount of time. 25

[0005] Another cancer detection method based on fluorescence imaging that eliminates the need to administer photosensitive drugs is based on the fact that cancerous or precancerous tissue responds differently to applied light than does normal tissue. When monochromatic light is applied to living tissue, a portion of the absorbed light will be re-emitted at different wavelengths in a process termed autofluorescence (also referred to as native fluorescence). If blue or ultraviolet light is applied to living tissue, the intensity or number of autofluorescence photons released by the abnormal tissue in the green portion of the visible light spectrum differs relative to the intensity or number of photons released by healthy tissue. In the red region of the visible light spectrum, the number of photons released by the healthy and abnormal tissue are closer to being similar. 30

[0006] Examples of prior art systems which utilize the difference in fluorescence and autofluorescence intensity to detect the presence of cancer cells include U. S. Patent No. 4,786,813 to Svanberg et al.; U.S. Patent No. 4,930,516 ('516) to Alfano et al.; U.S. Patent No. 5,042,494 ('494) to Alfano; U.K. Patent Application No. 2,203,831, by Zeng Kun; 35 U.S. Patent No. 5,131,398 ('398) to Alfano et al.; and PCT Application No. WO 90/10219 by Andersson-Engles.

[0007] The systems described in each of these patents generally fall into two categories in order to discriminate between cancerous and non-cancerous cells. The first category one utilizes single point, narrow band spectroscopy measurements to detect cancerous tissue, while the second utilizes broad band imaging systems. Examples of the systems in the first category are the Alfano patents, '516, '494 and '398, which describe single point measurement systems. These systems use a ratiometric comparison of the narrow band intensity of autofluorescence light produced by healthy and suspect tissue, as well as a detection of a change in spectral peaks (i.e., a shift towards the blue) to indicate the presence of cancerous cells. 40

[0008] However, these narrow band intensity measurements and the associated discrimination algorithm is based on an autofluorescence spectra derived from in vitro measurements of rat tumors that have not been found to be applicable to cancer in humans. The Zeng system simply looks for a change in the spectral envelope of the autofluorescence light to detect malignant tissue. However, this method has not proven sufficiently reliable to identify suspicious tissue in different patients due to changes in the amount of autofluorescence light produced as the probe is moved from one location to another or one patient to another. 45

[0009] Examples of the second category are illustrated by the Svanberg et al. and Andersson-Engles patents, which disclose systems for producing images of diseased tissue. The fluorescence or autofluorescence light produced by the tissue is divided into four beams that are filtered with a broadband filter before being applied to an intensified CCD camera. The output of the intensified CCD camera is used to compute ratios of the intensity of the four broad spectral bands. The ratio calculations are then displayed, typically as pseudo colors, on a monitor so that a physician can 50

visually detect the presence of cancerous lesions. However, the calculation of ratios or the requirement for image processing is not desirable in a medical diagnostic aid system because the physician loses information that is, in our experience, necessary for diagnostic judgment. Such information is only retained by presenting the physician with a view of the tissue directly and not a mathematical representation of the tissue.

[0010] A new development which leads to an apparatus for detecting the presence of cancerous tissue based on the differences in autofluorescence light is disclosed in our co-pending U.S. patent applications Serial Nos. 08/428,494 ('494), now U.S. Patent No. 5,507,287 and 08/218,662 ('662), now U.S. Patent No. 5,590,660. While the systems disclosed in the '494 and '662 applications constitute a significant advance in the field of cancer imaging, improvements can be made. For example, these systems require complex laser systems in order to produce the fluorescence excitation light. Although it is possible to use a relatively small ion laser, such as the HeCd laser, this has the disadvantage that the illumination power is not great enough for the examination of large cavity organs such as the colon and stomach. Furthermore, if fluorescence imaging is used together with white light reflectance imaging, an additional light source has to be used. Additionally, there are currently no cancer imaging systems that are designed to compensate for the changes of autofluorescence properties from patient to patient, from organ to organ, and from location to location. Finally, the manner in which cancerous or precancerous tissue is displayed does not take optimal advantage of the perceived color discrimination of the human eye.

[0011] The present invention is directed to address the problems of prior art cancer imaging systems and to improve the systems disclosed in the '494 and '662 applications in order to facilitate the detection of cancerous or precancerous tissue in the respiratory and gastrointestinal tracts.

## Summary of the Invention

[0012] The present invention is an imaging system for detecting the presence of cancerous or precancerous lesions in vivo. A light source produces (e.g. blue) excitation light that is directed into an illumination guide of a fiber optic endoscope in order to illuminate a portion of tissue to be examined. The endoscope returns some reflected excitation light as well as autofluorescence light produced by the tissue under examination. Light received from the endoscope, through the imaging fiber bundle, is divided into two beams by a beam splitter. The first beam comprises autofluorescence light in the green portion of the visible light spectrum as well as any reflected blue excitation light. The second beam comprises autofluorescence light in the red portion of the spectrum. Light in the two beams is filtered and applied to a pair of image intensified CCD cameras. Real time images (i.e., 30 frames/s), produced by the CCD cameras, are applied to the red, green and blue color inputs of a color video monitor. Still images can be captured from the real time images and stored by means of a frame grabber in a computer.

[0013] The blue and green color inputs of the video monitor are connected to receive the images produced by the camera that detects green autofluorescence light, while the red color input, of the color video monitor is connected to receive the image produced by the camera that detects the red autofluorescence light. The video monitor produces a display whereby normal tissue appears as approximately cyan in color, while potentially cancerous tissue appears reddish in color. It turns out that the perceived colors on the monitor represent the ratio of the two acquisition channels. This is an important aspect of the present invention since the ratio is displayed without calculations or digital image processing but by simply mixing the three color channels.

[0014] A further aspect of the invention is a pair of controls that allow a physician to adjust the brightness and color contrast of the video display image by adjusting the gain of the red and green intensified CCD cameras in a specific proportion to compensate for the changes in autofluorescence from patient to patient, from organ to organ, and from location to location.

[0015] Another aspect of the invention is an improvement to the excitation light source. A mercury arc lamp is used to produce the blue excitation light at the strong atomic line of 436 nanometers. Light from the arc lamp is gathered by an elliptical mirror and filtered by a dichroic mirror and a bandpass filter before it is directed into the illumination guide of the endoscope. This filtered light source gives high illumination power and is inexpensive to manufacture and is relatively easy to maintain.

## Brief Description of the Drawings

[0016] The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same becomes better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 is a graph showing the difference in autofluorescence intensity between normal and cancerous tissue; FIGURE 2 is a graph showing the difference in autofluorescence spectral shape between normal and cancerous tissue in the spectral bands utilized by the present invention;

FIGURE 3 is a block diagram of a cancer detection system according to the present invention;  
 FIGURE 4 is a block diagram of the image acquisition/processing units used with the cancer detection system of the present invention;  
 FIGURE 5 is a chromaticity diagram showing how the perceived color for normal and cancerous tissue are displayed by the cancer detection system of the present invention;  
 FIGURE 6 is a diagram of an excitation light source according to another aspect of the present invention; and  
 FIGURE 7 is a pictorial diagram of an image produced by the cancer detection system of the present invention.

#### Detailed Description of the Preferred Embodiment

[0017] The present invention is a system for detecting cancerous or precancerous tissues using autofluorescence images that does not require the use of tumor enhancing drugs or intensive image processing.

[0018] FIGURE 1 is a graph showing the differences in autofluorescence light intensity for normal and cancerous or precancerous tissue in humans. As indicated above, when blue excitation light is shined on tissue, some of the light will be absorbed and reemitted as autofluorescence light. The autofluorescence light has an intensity and spectral shape that is indicative of whether the tissue is normal or diseased. A spectral curve 10 represents the response of normal, healthy tissue, while a spectral curve 20 represents the response of tissue that is cancerous or precancerous. As can be seen, there is a significant difference in the intensity of the two curves in a first green channel 30, while the differences between the healthy and abnormal tissue in a second red channel 40 is small.

[0019] The magnitude of the curves 10 and 20 shown in FIGURE 1 not only vary with wavelength, but also with the distance between a probe and the tissue under examination as well as the intensity of the light source. Therefore, in a practical sense it is not possible to determine whether tissue is cancerous by simply detecting the magnitude of the autofluorescence light in the (first) green channel. However, the ratios of the autofluorescence light intensities taken at two different wavelengths remain constant despite variations in the distance of the fiber optic probe to the tissue and the angle of the probe to the tissue. This is true since the intensities of the (first) green and (second) red channel change proportionally for the same kind of tissue. That is, the intensity of red autofluorescence light for normal tissue  $R_n$  divided by the intensity of the green autofluorescence light for normal tissue  $G_n$  remains substantially constant despite variations in the distance and angle of the tip of the endoscope to the tissue under consideration. Similarly, the ratio of the intensity of the red autofluorescence light  $R_{cis}$  (CIS for carcinoma *in situ*) divided by the intensity of the green autofluorescence light  $G_{CIS}$  remains substantially constant despite variations in the position and orientation of the endoscope.

[0020] For healthy tissue, the inventors have found that the ratio of the response of the red channel to the green channel is approximately 0.54 for colon tissue and 0.16 for lung tissue, while for carcinoma *in situ*, the ratio of the red to green channel is approximately 1.6 for colon tissue and 0.6 for lung tissue. These values are given as examples only and they are highly dependent on the system, i.e., the spectral response of the imaging system. However, by calculating or by representing the ratio of the red channel autofluorescence light and the green channel autofluorescence light, a determination can be made whether the tissue under consideration is healthy or potentially cancerous when interpreted along with the contextual information of the image.

[0021] FIGURE 2 shows the range of wavelengths used by the present invention to determine whether tissue is potentially cancerous or precancerous. The (second) red channel 60 is limited to wavelengths longer than 630 nanometers, while the (first) green channel 50 comprises wavelengths extending from approximately 490 to 560 nanometers. To demonstrate that the spectral curves are different not only in intensity but also in shape, the areas in the red band have been normalized so that, in this part of the spectrum, the ratio of the normal and cancerous tissue is one. This normalization still results in a significant difference in the green band. Therefore, the ratio or a representation of the ratio will discriminate between normal and cancerous tissue. By simultaneously displaying the autofluorescence light received in each of these bands as a color image, the present invention allows a physician to determine whether the tissue under consideration is potentially cancerous or precancerous.

[0022] Turning now to FIGURE 3, the endoscope autofluorescence imaging system of the present invention includes an excitation light source 100 and a fiber optic endoscope 102, which may be a gastroscope, duodenoscope, choledochoscope, bronchoscope or colonoscope depending on the type of tissue to be examined. For example, the endoscope may be an Olympus BF-20D for the respiratory tract, an Olympus GIF-XQ30 for the esophagus and stomach and an Olympus CF-30L for the rectum and colon.

[0023] The light source 100 produces blue excitation light 104 which is fed through the incoherent illumination guide 106 of the fiber optic endoscope. The excitation light is focused by an outer lens 108 that is disposed at the distal end of the endoscope. When the endoscope is inserted into a body cavity by a physician, the blue excitation light illuminates a portion of tissue 110 that is to be examined. The tissue is excited by the blue light and emits photons (autofluorescence light) 112 having a longer wavelength in the visible portion of the light spectrum. The autofluorescence light emitted by the tissue along with some reflected blue excitation light is gathered by a lens 114 at the distal end of the endoscope

and channeled through an imaging guide portion 116 of the endoscope through a number of conventional imaging lenses (not shown).

[0024] After exiting the endoscope, autofluorescence light is applied to a dichroic mirror beam splitter 120. The beam splitter 120 has a cutoff wavelength between 565 and 575 nanometers. The beam splitter divides the autofluorescence light from the imaging guide into two spectral bands, namely a first, green band, and a second, red band. The autofluorescence light having wavelengths longer than the cutoff wavelength of the beam splitter 120 is directed toward a reflection mirror 122 that directs the autofluorescence light into a filter 124. The filter 124 is positioned in front of a red channel, image intensified CCD camera 126. Autofluorescence light having wavelengths less than the cutoff wavelength of the beam splitter 120 passes through the beam splitter toward a filter 128 that is positioned in front of a green channel image intensified CCD camera 130.

[0025] By separating the autofluorescence light gathered by the endoscope into the two spectral bands, virtually all photons having wavelengths in the red portion of the spectrum are supplied to the CCD camera 126 while virtually all photons having wavelengths in the green portion of the spectrum are applied to the CCD camera 130. As shown in Figure 1, the intensity of the red autofluorescence wavelength band that is applied to the camera 126 is substantially the same for normal tissue and abnormal tissue. However, the intensity of the green autofluorescence wavelength band applied to the camera 130 is substantially different for normal and abnormal tissue.

[0026] As will be described in further detail below, the images produced by both CCD cameras 126 and 130 are combined on a color video monitor 150 that allows any abnormal tissue to be easily identified. Because a high power blue excitation light is employed and all the photons in the spectral bands are applied to the image intensified CCD cameras 126 and 130, the images produced by the cameras 126 and 130 are bright enough to distinguish between normal and abnormal tissue, even in the larger organs such as in the gastrointestinal tract, without the need for tumor enhancing photosensitive drugs.

[0027] FIGURE 4 is a more detailed block diagram of the imaging portion of the cancer detection system according to the present invention. After the autofluorescence light 112 is either reflected by or passes through the dichroic mirror 120 (FIGURE 3), the light is directed to the filters 124 and 128. The filter 124 is a long pass filter that blocks light having wavelengths less than 630 nanometers. After passing through the long pass filter 124, the red autofluorescence light is directed onto the surface of a GEN II image intensifier 132 such as a DEP XX 1700 manufactured by Delft Instruments. The output of the image intensifier 132 is coupled through a fiber optic bundle 134 to the surface of a CCD image sensor 136 within the CCD camera 126.

[0028] The green autofluorescence light passes through a bandpass filter 128 that removes any blue excitation light that may have been reflected off the surface of the tissue 110. In the present embodiment of the invention, the bandpass filter 128 removes light having wavelengths less than 490 nanometers or greater than 560 nanometers. The out of band attenuation of the filters 124 and 128 must be sufficient to ensure that virtually all of the reflected blue excitation light is blocked from reaching the CCD cameras. After passing through the filter 128, the green autofluorescence light is directed to a GEN II image intensifier 140. The output of the image intensifier 140 is coupled via a fiber optic bundle 142 to the surface of a CCD image sensor 144 within the green CCD camera 130. A genlock 149 within the camera 130 maintains the synchronization of the red CCD camera 126 to the green CCD camera 130.

[0029] The analog output signals of the red and green image intensified CCD cameras 126 and 130 are fed to a pair of amplifiers 152, 154. The output of the amplifiers is fed into a video image processing board 155 that is part of a controlling computer 200. The controlling computer 200 includes an Intel 486/100MHz CPU 202 and 16 US of internal memory 204. However, other high speed digital computers could also be used.

[0030] The video image processing board 155 includes a pair of analog-to-digital converters 156, 157, that receive the amplified video signals from the red and green CCD cameras, respectively. The analog-to-digital converters convert the analog video signals into a corresponding digital format. After being digitized, a pair of look up tables 158 and 160 are used to modify the relative gain of the digital video signals in a manner that will be described below. For each discrete value of the digital video signal, the CPU 202 reads up a corresponding digital value having the correct relative gain from the look up tables. The values of the digitized video signals read from the look up tables 158, 160, that are part of a random access memory 162 where they can be retrieved by the central processing unit for analysis at a later time.

[0031] To display the image signals in real time, the digital video signals are continuously retrieved from the random access memory 162 and reconverted into an analog format by a pair of digital-to-analog converters 166 and 164. The two converters correspond respectively to the green and red channel images. The outputs of the digital to analog converters 164, 166, are applied directly to the red, green and blue inputs of the color monitor 150 shown in FIGURE 3. This means that the video signal from the green CCD camera 130 is coupled to a green input 150G of the color monitor as well as a blue input 150B. A red input 150R of the color monitor receives the video signal from the red CCD camera 126.

[0032] The color video monitor 150 receives the video signals and produces a color image, whereby the healthy tissue is approximately cyan in color and any abnormal or potentially cancerous tissue appears reddish in color and

is therefore easily identifiable by a trained physician.

[0033] The direct coupling of the video signals from the video input/output board of cameras 126, 130 through the video image processing board 155 to the color video monitor 150 is accomplished without any significant digital signal processing other than a minor change in the gain as will be described below. This allows a physician to view as true a representation of the data from the intensified CCD cameras as possible. In other words, the structure (e.g., contrast and texture) of the image are maintained. Therefore, the physician is able to consider subtleties in the video image that may otherwise be removed or masked as a result of any digital image processing that takes place before the image is displayed. The two autofluorescence image signals produced by the CCD cameras are representative of the true autofluorescence image of the tissue in the respective wavelength bands, allowing lesions to be seen at video rates within their context. This aspect is essential for the physician to recognize potential lesions which he/she can then biopsy through the biopsy channel of the endoscope for pathology confirmation.

[0034] The fluorescence imaging system of the present invention is unique in that it does not perform calculations to compensate for distance and angle effects of the endoscope with respect to the tissue under examination. Instead, the images from the red and green cameras are superimposed upon each other and displayed as distinct colors. This allows the physician to interpret the image using the visual experience they have acquired over their lifetime. In addition, the system circumvents the problem of an algorithm making a clinical decision as to what tissue may or may not be cancerous as well as allows the tissue to be observed in real time.

[0035] The inventors have found that the autofluorescence properties of tissue change from patient to patient, from organ to organ, and from location to location. Therefore, the present invention provides a set of controls 220 that allow the physician to adjust the "brightness" and "color balance" of the color video image produced. The controls 220 can be realized by hardware or software control of the camera gain.

[0036] The brightness of the displayed image is related to the gain of both the red and green channels while the color balance is related to the relative gain of the green and red channels. In the presently preferred embodiment of the invention, the gain of the red channel camera 126 is related to the gain of the green channel camera 130 according to the equation:

$$R_{(G)} = aG^2 + bG + c \quad (1)$$

where R is the gain of the red channel image intensifier and G is the gain of the green channel image intensifier, and a, b and c are constant. As will be appreciated, the particular values selected for the constants a, b and c depend on the type of intensified CCD camera used, the intensity of the light source, the properties of the tissue and the human eye's ability to perceive color. However, for the system described above, the inventors have found that the constant "a" should be selected in the range of 0.0 to 0.1, "b" should be in the range of 0.5 to 1.5, and "c" should be selected from the range of 0.0 to 0.5.

[0037] The constant "c" provides for an offset in color between the two channels while the linear term "b" ensures that as the overall brightness is changed, the gain of both the green and red channels is related. The quadratic term "a" provides a second order connection to ensure that the perceived color on the monitor remains the same despite variations to the overall brightness of the display. However, in the present embodiment of the invention, the "a" term is set to zero.

[0038] To adjust the brightness of the image displayed on the monitor, the physician adjusts the position of a knob 222 which adjusts the gain of the green channel. Movement of this knob 222 produces signals on a lead 224 that are read by the CPU 202. The CPU 202 then adjusts the numbers stored in the look up tables 158 and 160 according to Equation 1 without changing the values of the constants a, b and c. Alternatively, the CPU can adjust the gain of the red and green intensified CCD cameras by supplying gain signals from the CPU to a pair of gain control boards 146, 148, which control the high voltage of the image intensifiers 132, 140. As will be appreciated, as the gain of the green channel is increased or decreased, the gain of the red channel is increased or decreased proportionally.

[0039] To adjust the color balance of the image, the physician adjusts the position of a contrast knob 226. Movement of the knob 226 produces signals on a lead 228 that are read by the CPU 202. The CPU then adjusts the multiplier b that relates the gain of the red channel to the gain of the green channel. In the present embodiment of the invention, the constant "b" is varied linearly in the range described above as the contrast control knob 226 is moved between its minimum and maximum positions. The CPU then calculates a gain of the red channel by recalculating the values stored in the look up table 158 or adjusts the gain of the red channel image intensifier camera 132 by supplying a new gain signal to the gain control board 146.

[0040] In practice, the physician adjusts the brightness control knob 222 until an image of sufficient intensity of the tissue is produced on the video monitor 150. If the physician believes he or she is viewing a malignant lesion, the position of the color balance knob 226 is adjusted until the entire video image appears red. The color balance knob

can be readjusted until no red is apparent in the background of the video image. If the area of interest still appears reddish in color, the physician can have greater certainty that the red portion of the video image is a cancerous or precancerous lesion. The color balance control knob 226 can also be adjusted so that the displayed color is what the physician wants to see, thereby giving the physician some flexibility in setting the display to be something that is easier for the individual physician to interpret.

[0041] As indicated above, the present invention displays tissue on the color monitor as a color that is not dependent upon the position or orientation of the endoscope with respect to the tissue under examination. The rationale as to why this is true for the present invention is stated below.

[0042] In general, any RGB color monitor can be modeled according to the following equation:

$$\begin{bmatrix} X \\ Y \\ Z \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix} \begin{bmatrix} R \\ G \\ B \end{bmatrix} \quad (2)$$

[0043] The values R, G and B are the magnitudes of the video signals applied to the color inputs of the monitor and the 3x3 matrix comprises a series of fixed coefficients that are primarily determined by the phosphor used on the monitor. The values, X, Y and Z are referred to as tristimulus values.

[0044] Every color that can be displayed on the monitor can be represented as a pair of color coordinates x, y, on a chromaticity diagram 250 as shown in FIGURE 5. This is a widely used conventional diagram used to represent colors that can be displayed on a video monitor. The coordinates x and y are related to the tristimulus values by the equations:

$$x = \frac{X}{X + Y + Z} \quad (3)$$

$$y = \frac{Y}{X + Y + Z} \quad (4)$$

[0045] The Television Engineering Handbook by K. Blair Benson (McGraw Hill, 1992) is a typical reference where these equations and definition of the chromaticity diagram can be found.

[0046] Since, for the present invention, the green signal G is fed into the blue channel,  $G = B$ , one can expand Equations 2 and 3 arriving at the following:

$$x = \frac{a_{11}R + (a_{12} + a_{13})G}{(a_{11} + a_{21} + a_{31})R + (a_{12} + a_{22} + a_{23} + a_{13} + a_{32} + a_{33})G} \quad (5)$$

[0047] Similarly, expanding Equations 2 and 4, gives the following:

$$y = \frac{a_{21}R + (a_{22} + a_{23})G}{(a_{11} + a_{21} + a_{31})R + (a_{12} + a_{22} + a_{23} + a_{32} + a_{33})G} \quad (6)$$

[0048] For the cancer detection systems of the present invention, it has been determined that the ratio of the red to green autofluorescence intensity remains the same for a given tissue regardless of the intensity of the excitation light, orientation of the probe, or distance of the probe to the tissue under examination. If the  $R/G$  is a constant, i.e.,  $R/G = k$ , x of Equation 5 and y of Equation 6 will remain constant. Hence, the color shown on the monitor 150 will be constant regardless of how the probe is positioned within the patient. The only time the ratio between the red and green autofluorescence light changes and hence the only time the color on the video monitor changes is when the tissue under examination is potentially cancerous (since in that case, the ratio  $R/G$  changes due to the different spectral response). Therefore, a physician needs only to look for variations in the color of the display to detect potentially cancerous lesions.

[0049] It has been determined that for the cancer detection system described above, the ratio of the red to green autofluorescence light for healthy colon tissue is approximately 0.54. When the color coordinates x and y, of the chromaticity graph, are computed and plotted for Equations 3 and 4 given that for a constant  $R/G$  ratio of 0.54, as shown in FIGURE 5, it results in a point 252 having coordinates  $x_1, y_1$  with a greenish hue. Similarly, it has been determined that the ratio of the red to green autofluorescence light for potentially cancerous colon tissue is approximately 1.6

which, when plotted, results in a point 254 having coordinates  $x_2, y_2$  with a red-brown hue.

[0050] About each point on the chromaticity graph lies an area 256, 258, 264 and 266 about which the human eye cannot perceive changes in color. It has further been determined that these areas tend to decrease in size as the value of  $x, y$  decreases, i.e., the colors shown in the blue to red region of the chromaticity diagram. By feeding the green autofluorescence signal into both the blue and green inputs of the color monitor, the position of point 252 moves to a point 260, having coordinates  $x_3, y_3$ , in the blue region of the chromaticity graph. Similarly, the point 254 is moved to a point 262, having coordinates  $x_4, y_4$ , near the red region of the graph. Because the colors displayed are in an area where the human eye is more perceptive of slight color changes, a physician is more easily able to detect slight variations in color and, hence, can more readily detect potentially cancerous tissue.

[0051] To display the R/G ratio as a color is an important part of the present invention. In the prior art it is difficult to calculate and display the ratio in real time video rates of 30 frames per second. In addition, the display of a calculated ratio does not provide contextual information. Contextual information is, in our experience, essential to allow a physician to determine whether a suspicious lesion requires a biopsy or whether or not an artifact is observed (e.g., blood). The color display system of the present invention is fast because no calculations are performed and the resulting image retains the tissue contextual information.

[0052] FIGURE 6 is a schematic diagram of the excitation light source 100 shown in FIGURE 1. The light source 100 produces an intense blue light at the 436 nanometer mercury-atomic line that is used to illuminate large internal body cavities. The light source includes a one hundred watt mercury arc lamp 300 that produces light having a significant blue spectral content. The inventors have found that in order to couple the blue light produced by the lamp 300 into the illumination guide 106 of the endoscope, the arc size of the lamp must be smaller than the diameter of the illumination guide of the endoscope. In the preferred embodiment of the invention, the arc lamp used is an Ushio model number USH-102D having arc dimensions of approximately 0.25 millimeters.

[0053] Surrounding the arc lamp 300 is a collecting mirror 302, which in the present embodiment of the invention is elliptical in shape. The arc lamp 300 is positioned at one focus of the mirror 302 so that light from the sides and rear of the lamp 300 is gathered by the mirror and directed towards a dichroic mirror 303. In this way, as much as 80% of the radiation energy of the lamp is collected. The dichroic mirror 303 is preferably mounted below the arc lamp 300 at a position closer than the second focus of the elliptical mirror. Light having wavelengths between 350 and 450 nanometers is reflected at forty-five degrees from the face of the dichroic mirror 303 and through a 399 nanometer, low fluorescence, long pass filter 306. In addition to reflecting light in the desired spectral band, the dichroic mirror 303 also serves to pass longer wavelengths of light to a beam stop 305 allowing one to filter out the infrared radiation so that components of the light source do not suffer thermal damage. A shutter 304 positioned between the dichroic mirror 303 and a long pass filter 306 is used to control whether the excitation input is directed into the endoscope.

[0054] The long pass filter 306 attenuates the strong spectral lines produced by the mercury arc lamp in the ultraviolet range so that a coating on an interference bandpass filter 310 described below is protected from damage. After passing through the long pass filter 306, the light is directed to a one hundred millimeter focal length plano convex lens 308 that creates an optically homogenous, substantially parallel light beam, which is necessary for high out-of-band rejection filtering by a color filter 310.

[0055] The color filter, which preferably comprises an interference bandpass filter, is positioned perpendicular to the light beam produced by the lens 308 to attenuate light having wavelengths less than 400 nanometers and greater than 450 nanometers.

[0056] In the present embodiment of the invention, the dichroic mirror 303 reflects about 10% of the light outside the band of 350-450 nanometer band. Because a very pure excitation light is required for tissue fluorescence imaging, the interference bandpass filter 310 is used to further reduce the amount of light outside of the interested wavelength band (420 nanometers to 450 nanometers). The bandpass filter 310 has an out of band transmittance of smaller than  $5 \times 10^{-5}$  so that light with wavelengths less than 420 nanometers or greater than 450 nanometers is weaker than the autofluorescence light emitted from the tissue.

[0057] After passing through the interference bandpass filter 310, the remaining light is directed to a 65 millimeter focal length lens 312 that focuses the light onto an end of the illumination guide 106 (FIGURE 3).

[0058] The light source 100 shown in FIGURE 6 provides approximately 500 milliwatts of blue light into the illumination guide of the endoscope. This light is sufficient to illuminate large internal body cavities such as the stomach or colon. The light source delivers approximately 50-80 milliwatts of excitation light at the end of the endoscope in contrast to the 15 milliwatts that are typically delivered with a laser light source. In addition, the light source 100 is easier to manufacture and maintain than a laser.

[0059] FIGURE 7 is a pictorial representation of an image produced by the cancer detection system of the present invention. As indicated above, the video monitor 150 produces a color display, wherein healthy tissue appears cyan (white-blue) in color and potentially cancerous or precancerous lesions appear reddish brown. The video display produced thereby allows physicians to readily detect the presence of cancerous or precancerous lesions without the use of photosensitive drugs. In addition, the color display retains the contextual information of the tissue, thereby allowing



the physician to interpret subtleties in the image that are traditionally lost in digital camera systems that employ significant digital signal processing. The cancer detection system of the present invention is ideally suited for cancer screening applications whereby it is desired to test as many patients as possible for the presence of abnormal tissue without need to administer photosensitive drugs.

[0060] While the preferred embodiment of the invention has been illustrated and described, it will be appreciated that various changes can be made therein without departing from the scope of the invention. It is therefore intended that the scope of the invention be determined solely from the following claims.

## 10 Claims

### 1. Apparatus for imaging tissue using autofluorescence comprising:

a light source (100) for generating excitation light (104) that will cause tissue to generate characteristic autofluorescence light (112);  
 means (106, 108) for illuminating tissue (110) with the excitation light (104) thereby exciting tissue to emit said characteristic autofluorescence light (112);  
 collecting means (114, 116) for gathering reflected excitation light and said characteristic emitted autofluorescence light (112) produced by the tissue (110);  
 a beam splitter (120) positioned to receive the reflected excitation light and the emitted autofluorescence light (112) collected by the collecting means (114, 116), the beam splitter (120) operating to separate the spectral components of said autofluorescence light into at least a first spectral band (30, 50) including the reflected excitation light and emitted autofluorescence light having wavelengths where an autofluorescence intensity ( $G_{CIS}$ ) for abnormal tissue is substantially different from an autofluorescence intensity ( $G_n$ ) for normal tissue and a second spectral band (40, 60) different from said first spectral band (30, 50) including the emitted autofluorescence light having wavelengths where an autofluorescence intensity ( $R_{CIS}$ ) for abnormal tissue is substantially similar to that of ( $R_n$ ) normal tissue;  
 a first optical filter (128) positioned to receive the light within the first spectral band (30, 50), said first filter (128) operating to remove the reflected excitation light from the light within the first spectral band;  
 a second optical filter (124) positioned to receive the light within the second spectral band (40, 60);  
 a first camera (130) for receiving the autofluorescence light within the first spectral band (30, 50) and for producing a first autofluorescence image signal of the tissue;  
 a second camera (126) for receiving the autofluorescence light within the second spectral band (40, 60) and for producing a second autofluorescence image signal of the tissue;  
 a color monitor (150) having at least a first (150G) and a second (150R) color input, whereby the first color input (150G) is coupled to receive the first autofluorescence image signal and the second color input (150R) is coupled to receive the second autofluorescence image signal to create a combined, display image in which said abnormal and normal tissue are displayed on the color monitor (150); and

characterized by the provision of a control (202, 222) for adjusting the gain of one of the first or second autofluorescence image signals produced by the cameras (130, 126) as a function of the gain of the other of the first or second autofluorescence image signals.

### 2. Apparatus according to Claim 1, wherein the light source (100) includes:

a) a lamp (300) that produces excitation light;  
 b) a collecting mirror (302) positioned about the lamp (300) for collecting the excitation light produced by the lamp (300) and directing the excitation light outwardly of the collecting mirror (302);  
 c) a light source dichroic mirror (303) positioned to receive the excitation light collected by the collecting mirror (302) and to filter the excitation light;  
 d) a first lens (308) positioned to receive the filtered excitation light reflected from the first dichroic mirror (302) in order to produce a substantially parallel beam of excitation light;  
 e) a light source color filter (310) positioned to receive the parallel beam of excitation light, such color filter (310) operating to filter light having wavelengths not at the excitation wavelength from the parallel beam of excitation light; and  
 f) a second lens (312) positioned to receive the filtered beam of excitation light that has passed through the color filter (310), the second lens (312) focusing the excitation light into the endoscope (102) in order to excite the tissue (110) under examination.

3. Apparatus according to Claim 1 or 2, wherein the light source (100) includes a mercury arc lamp (300).
4. Apparatus according to Claim 3, wherein the collecting mirror (302) is an elliptical mirror positioned so that the mercury arc lamp (300) is at a focus of the elliptical mirror (302).
5. Apparatus according to Claim 3 or 4, wherein the excitation wavelength is 436 nanometers and the light source dichroic mirror (303) reflects excitation light having wavelengths between 350 and 450 nanometers.
6. Apparatus according to any preceding Claim, wherein the light source color filter (310) is an interference bandpass filter that passes excitation light having wavelengths between 420 and 450 nanometers.
7. Apparatus according to any preceding Claim, further comprising a bandpass filter (128) disposed between the beam splitter (120) and the first camera (130), and arranged to pass autofluorescence light having wavelengths between 490 and 560 nanometers.
8. Apparatus according to any preceding Claim, further comprising a red long pass filter (124) disposed between the beam splitter (120) and the second camera (126), the long pass filter (124) having a cutoff wavelength of 630 nanometers.
9. Apparatus according to any preceding Claim, wherein the color monitor (150) is an RGB monitor having red, green and blue color video inputs (150R, 150G, 150B).
10. Apparatus according to any preceding Claim, wherein the first (130) and second (126) cameras are image intensified CCD cameras.
11. Apparatus according to any preceding Claim, further comprising a control (202, 226) for adjusting the function by which the gain of the first or second autofluorescence image signal is dependent on the gain of the other of the first or second autofluorescence image signal.
12. Apparatus according to any preceding Claim, wherein said light source (100) is a source of substantially monochromatic light.
13. A system for detecting cancerous or precancerous tissue comprising apparatus according to any preceding Claim and including:
  - a substantially monochromatic light source (100) for producing excitation light (104) that causes tissue (110) under examination to produce autofluorescence light;
  - an endoscope (102) positioned to receive the excitation light and to direct the excitation light (104) into an internal body cavity of a patient and onto the tissue (110) under examination;
  - means (114, 116) for collecting the autofluorescence light (112) produced by the tissue (110) under examination;
  - the said beam splitter (120) adapted for dividing the collected autofluorescence light into a first beam having wavelengths where an intensity ( $G_{CIS}$ ) of the autofluorescence light from abnormal tissue is substantially different than that ( $G_n$ ) from normal tissue and a second beam having wavelengths where an intensity ( $R_{CIS}$ ) of the autofluorescence light from abnormal tissue is substantially the same as that ( $R_n$ ) from normal tissue;
  - a first (130) and second (126) image intensified or non-intensified CCD camera for receiving the first and second beams of autofluorescence light, respectively, the first and second image intensified or non-intensified CCD cameras (130, 126) producing a first and second autofluorescence image signal; and
  - said color monitor (150) having a red, blue and green color input, the red color input (150R) being connected to receive one of the first or second autofluorescence image signals and the blue and green color inputs (150B, 150G) being connected to receive the other of the first or second autofluorescence image signals in order to produce a display having a color that is representative of a ratio of a magnitude of the first autofluorescence signal and the second autofluorescence signal, said display providing an indication of whether the tissue is normal or abnormal.

## Patentansprüche

## 1. Vorrichtung zum Abbilden von Gewebe unter Einsatz von Autofluoreszenz, umfassend:

- 5 eine Lichtquelle (100) zum Erzeugen von Anregungslicht (104), welches das Gewebe dazu bringt, charakteristisches Autofluoreszenzlicht (112) zu erzeugen;
- eine Einrichtung (106, 108) zum Beleuchten von Gewebe (110) mit dem Anregungslicht (104), um dadurch das Gewebe dazu anzuregen, das charakteristische Autofluoreszenzlicht (112) zu emittieren;
- 10 eine Aufnahmeeinrichtung (114, 116) zum Sammeln von reflektiertem Anregungslicht und von dem charakteristischen, emittierten Autofluoreszenzlicht (112), das von dem Gewebe (110) erzeugt wird;
- einen Strahlteiler (120), der so angeordnet ist, daß er das reflektierte Anregungslicht und das emittierte Autofluoreszenzlicht (112), das von der Aufnahmeeinrichtung (114, 116) gesammelt wurde, empfängt, wobei der Strahlteiler so arbeitet, daß er die Spektralkomponenten des Autofluoreszenzlichts auf trennt in mindestens ein erstes spektrales Band (30, 50), welches das reflektierte Anregungslicht und emittiertes Autofluoreszenzlicht mit Wellenlängen enthält, bei denen eine Autofluoreszenz-Intensität ( $G_{CIS}$ ) für krankhaftes Gewebe wesentlich verschieden ist von einer Autofluoreszenz-Intensität ( $G_n$ ) für normales Gewebe, und ein zweites spektrales Band (40, 60), das sich von dem ersten spektralen Band (30, 50) unterscheidet und das emittierte Autofluoreszenzlicht mit Wellenlängen enthält, bei denen eine Autofluoreszenz-Intensität ( $R_{CIS}$ ) für krankhaftes Gewebe im wesentlichen derjenigen ( $R_n$ ) für normales Gewebe ähnelt,
- 15 ein erstes optisches Filter (128), positioniert zur Aufnahme des Lichts innerhalb des ersten spektralen Bands (30, 50), wobei das erste Filter (128) so arbeitet, daß es aus dem Licht innerhalb des ersten spektralen Bands das reflektierte Anregungslicht entfernt;
- 20 ein zweites optisches Filter (124), positioniert zum Aufnehmen des Lichts innerhalb des zweiten spektralen Bands (40, 60);
- 30 eine erste Kamera (130) zum Aufnehmen des Autofluoreszenzlichts innerhalb des ersten spektralen Bands (30, 50) und zum Erzeugen eines ersten Autofluoreszenzbildsignals des Gewebes;
- eine zweite Kamera (126) zum Aufnehmen des Autofluoreszenzlichts innerhalb des zweiten spektralen Bands (40, 60) und zum Erzeugen eines zweiten Autofluoreszenzbildsignals des Gewebes;
- 35 einen Farbmonitor (150) mit mindestens einem ersten (150G) und einem zweiten (150R) Farbeingang, von denen der erste Farbeingang (150) so verschaltet ist, daß er das erste Autofluoreszenzbildsignal empfängt, und der zweite Farbeingang (150R) so verschaltet ist, daß er das zweite Autofluoreszenzbildsignal empfängt, um ein kombiniertes Anzeigebild zu erzeugen, in welchem das krankhafte und normale Gewebe auf dem Farbmonitor (150) angezeigt sind; und
- 40 **gekennzeichnet durch** die Bereitstellung einer Steuerung (202, 222) zum Einstellen der Verstärkung des einen Signals von dem ersten und dem zweiten Autofluoreszenzbildsignal, die von den Kameras (130, 126) erzeugt werden, als eine Funktion der Verstärkung des anderen Signals von dem ersten und dem zweiten Autofluoreszenzbildsignal.
- 45

## 2. Vorrichtung nach Anspruch 1, bei der die Lichtquelle (100) aufweist:

- 50 a) eine Anregungslicht erzeugende Lampe (300);
- b) einen Sammelspiegel (302), der um die Lampe (300) herum angeordnet ist, um das von der Lampe (300) erzeugte Anregungslicht zu sammeln und das Anregungslicht nach außerhalb des Sammelspiegels (302) zu lenken,
- 55 c) einen dichroitischen Lichtquellen-Spiegel (303), positioniert zum Aufnehmen des von dem Sammelspiegel (302) gesammelten Anregungslichts und zum Filtern des Anregungslichts;

d) eine erste Linse (308), positioniert zum Aufnehmen des gefilterten Anregungslichts, welches von dem ersten dichroitischen Spiegel (302) reflektiert wird, um ein im wesentlichen paralleles Strahlbündel aus Anregungslicht zu erzeugen;

e) ein Lichtquellen-Farbfilter (310), positioniert zum Aufnehmen des parallelen Anregungslicht-Strahlbündels, wobei dieses Farbfilter (310) so arbeitet, daß es aus dem parallelen Anregungslicht-Strahlbündel solche Wellenlängen herausfiltert, die nicht bei der Anregungswellenlänge liegen; und

f) eine zweite Linse (312), positioniert zum Aufnehmen des gefilterten Anregungslicht-Strahlbündels, das das Farbfilter (310) durchlaufen hat, wobei die zweite Linse (312) das Anregungslicht in ein Endoskop (102) fokussiert, um das untersuchte Gewebe (110) anzuregen.

3. Vorrichtung nach Anspruch 1 oder 2, bei der die Lichtquelle (100) eine Quecksilberdampfampe (300) enthält.

4. Vorrichtung nach Anspruch 3, bei der der Sammelspiegel (302) ein elliptischer Spiegel ist, derart positioniert, daß die Quecksilberdampfampe (300) sich im Brennpunkt des elliptischen Spiegels (302) befindet.

5. Vorrichtung nach Anspruch 3 oder 4, bei der die Anregungswellenlänge 436 Nanometer beträgt und der dichroitische Lichtwellenspiegel (303) Anregungslicht mit Wellenlängen zwischen 350 und 450 Nanometer reflektiert.

6. Vorrichtung nach einem vorhergehenden Anspruch, bei der das Lichtquellen-Farbfilter (310) ein Interferenz-Bandpaßfilter ist, welches Anregungslicht mit Wellenlängen zwischen 420 und 450 Nanometer durchläßt.

7. Vorrichtung nach einem vorhergehenden Anspruch, weiterhin umfassend ein Bandpaßfilter (128) zwischen dem Strahlteiler (120) und der ersten Kamera (130), ausgebildet zum Durchlassen von Autofluoreszenzlicht mit Wellenlängen zwischen 490 und 560 Nanometer.

8. Vorrichtung nach einem vorhergehenden Anspruch, weiterhin umfassend ein Rot-Langpaßfilter (124) zwischen dem Strahlteiler (120) und der zweiten Kamera (126), wobei das Langpaßfilter (124) eine Grenzwellenlänge von 630 Nanometer besitzt.

9. Vorrichtung nach einem vorhergehenden Anspruch, bei der der Farbmonitor (150) ein RGB-Monitor mit einem Rot-, einem Grün- und einem Blau-Farbvideoeingang (150R, 150G, 150B) ist.

10. Vorrichtung nach einem vorhergehenden Anspruch, bei der die erste (130) und die zweite (126) Kamera bildverstärkte CCD-Kameras sind.

11. Vorrichtung nach einem vorhergehenden Anspruch, weiterhin umfassend eine Steuerung (202, 226) zum Einstellen der Funktion, gemäß der die Verstärkung des ersten oder des zweiten Autofluoreszenzbildsignals von der Verstärkung des anderen Signals von dem ersten und dem zweiten Autofluoreszenzbildsignals abhängt.

12. Vorrichtung nach einem vorhergehenden Anspruch, bei der die Lichtquelle (100) eine Quelle von im wesentlichen monochromatischem Licht ist.

13. System zum Nachweisen von krebsartigem oder präkanzerösem Gewebe, umfassend eine Vorrichtung nach einem vorhergehenden Anspruch, und enthaltend:

eine im wesentlichen monochromatische Lichtquelle (100) zum Erzeugen von Anregungslicht (104), welches untersuchtes Gewebe (110) veranlaßt, Autofluoreszenzlicht zu erzeugen;

ein Endoskop (102), derart positioniert, daß es das Anregungslicht aufnimmt und das Anregungslicht (104) in einen inneren Körperhohlraum eines Patienten und auf das untersuchte Gewebe (110) lenkt;

eine Einrichtung (114, 116) zum Aufnehmen des von dem untersuchten Gewebe (110) erzeugten Autofluoreszenzlichts (112);

wobei der Strahlteiler (120) dazu ausgebildet ist, das aufgenommene Autofluoreszenzlicht aufzutellen in ein erstes Strahlbündel mit Wellenlängen, bei denen eine Intensität ( $G_{CIS}$ ) des von krankhaftem Gewebe kommenden Au-

tofluoreszenzlichts wesentlich verschieden ist von derjenigen ( $G_n$ ) normalen Gewebes, und ein zweites Strahlbündel mit Wellenlängen, bei denen eine Intensität ( $R_{CIS}$ ) des von krankhaftem Gewebe kommenden Autofluoreszenzlichts im wesentlichen die gleiche ist wie diejenige ( $R_n$ ) von normalen Gewebe;  
 eine erste (130) und eine zweite (126) bildverstärkte oder nicht-verstärkte CCD-Kamera zum Aufnehmen des ersten und des zweiten Autofluoreszenzlicht-Strahlbündels, wobei die erste und zweite bildverstärkte oder nicht-verstärkte CCD-Kamera (130, 126) ein erstes bzw. ein zweites Autofluoreszenzbildsignal erzeugen;  
 wobei der Farbmonitor (150) einen Rot-, einen Blau- und einen Grün-Färbeingang besitzt, von denen der Rot-Färbeingang (150R) verschaltet ist zum Aufnehmen eines Signals von dem ersten und dem zweiten Autofluoreszenzbildsignal, und der Blau- und der Grün-Färbeingang (150B, 150G) so verschaltet sind, daß sie das andere Signal von dem ersten und dem zweiten Autofluoreszenzbildsignal empfangen, um eine Anzeige mit einer Farbe zu erzeugen, die repräsentativ ist für ein Verhältnis einer Stärke des ersten Autofluoreszenzsignals und des zweiten Autofluoreszenzsignals, wobei die Anzeige angibt, ob das Gewebe normal oder krankhaft ist.

## 15 Revendications

### 1. Appareil d'imagerie des tissus par autofluorescence comprenant :

une source de lumière (100) destinée à générer une lumière d'excitation (104) qui va provoquer l'émission par les tissus d'une lumière d'autofluorescence caractéristique (112) ;  
 des moyens (106, 108) d'illumination des tissus (110) grâce à la lumière d'excitation (104), excitant ainsi les tissus pour qu'ils émettent ladite lumière d'autofluorescence caractéristique (112) ;  
 des moyens de réception (114, 116) destinés à capturer la lumière d'excitation réfléchie et ladite lumière d'autofluorescence caractéristique émise (112) produite par les tissus (110) ;  
 une lame séparatrice (120) positionnée de manière à recevoir la lumière d'excitation réfléchie et la lumière d'autofluorescence émise (112) recueillies par les moyens de réception (114, 116), la lame séparatrice (120) fonctionnant de façon à séparer les composants spectraux de ladite lumière d'autofluorescence pour former au moins une première bande spectrale (30, 50) comprenant la lumière d'excitation réfléchie et la lumière d'autofluorescence émise ayant des longueurs d'ondes telles qu'une intensité de l'autofluorescence ( $G_{CIS}$ ) des tissus anormaux est notablement différente d'une intensité de l'autofluorescence ( $G_n$ ) des tissus normaux et une seconde bande spectrale (40, 60) différente de ladite première bande spectrale (30, 50) comprenant la lumière d'autofluorescence émise ayant des longueurs d'ondes telles qu'une intensité de l'autofluorescence ( $R_{CIS}$ ) des tissus anormaux est sensiblement la même que celle des tissus normaux ( $R_n$ );  
 un premier filtre optique (128) positionné de manière à recevoir la lumière de la première bande spectrale (30, 50), ledit premier filtre (128) fonctionnant de façon à éliminer la lumière d'excitation réfléchie de la lumière dans la première bande spectrale ;  
 un second filtre optique (124) positionné de manière à recevoir la lumière de la seconde bande spectrale (40, 60) ;  
 une première caméra (130) destinée à recevoir la lumière d'autofluorescence dans la première bande spectrale (30, 50) et à produire un premier signal d'image d'autofluorescence des tissus ;  
 une seconde caméra (126), destinée à recevoir la lumière d'autofluorescence dans la seconde bande spectrale (40, 60) et à produire un second signal d'image d'autofluorescence des tissus ;  
 un moniteur couleur (150) ayant au moins une première (150G) et une seconde (150R) entrée de couleur, par lequel la première entrée de couleur (150G) est couplée pour recevoir le premier signal d'image d'autofluorescence et la seconde entrée de couleur (150R) est couplée pour recevoir le second signal d'image d'autofluorescence pour créer une image sur écran combinée dans laquelle lesdits tissus anormaux et normaux apparaissent sur le moniteur couleur (150); et

caractérisé par la fourniture d'une commande (202, 222) destinée à ajuster le gain de l'un du premier ou du second signal d'image d'autofluorescence produits par les caméras (130, 126) en fonction du gain de l'autre du premier ou second signal d'image d'autofluorescence.

### 2. Appareil selon la revendication 1, dans lequel la source de lumière (100) comprend :

- a) une lampe (300) produisant une lumière d'excitation ;
- b) un miroir de collection (302) positionné vers la lampe (300) recueillant la lumière d'excitation produite par la lampe (300) et dirigeant la lumière d'excitation vers l'extérieur du miroir de collection (302) ;
- c) un miroir dichroïque de source de lumière (303) positionné de manière à recevoir la lumière d'excitation

recueillie par le miroir de collection (302) et à filtrer la lumière d'excitation ;

d) une première lentille (308) positionnée de manière à recevoir la lumière d'excitation filtrée réfléchiée depuis le premier miroir dichroïque (302) pour produire un faisceau essentiellement parallèle de lumière d'excitation ;

e) un filtre coloré de la source de lumière (310) positionné de manière à recevoir le faisceau parallèle de lumière d'excitation, lequel filtre coloré (310) fonctionnant de façon à filtrer la lumière ayant des longueurs d'onde n'étant pas à la longueur d'onde d'excitation du faisceau parallèle de lumière d'excitation ; et

f) une seconde lentille (312) positionnée de manière à recevoir le faisceau de lumière d'excitation filtré qui est passé à travers le filtre coloré (310), la seconde lentille (312) focalisant la lumière d'excitation dans l'endoscope (102) pour exciter les tissus (110) sous examen.

3. Appareil selon la revendication 1 ou 2, dans lequel la source de lumière (100) comprend une lampe à arc au mercure (300).

4. Appareil selon la revendication 3, dans lequel le miroir de collection (302) est un miroir elliptique positionné de manière à ce que la lampe à arc au mercure (300) soit au foyer du miroir elliptique (302).

5. Appareil selon la revendication 3 ou 4, dans lequel la longueur d'onde d'excitation est de 436 nanomètres et le miroir dichroïque de la source de lumière (303) réfléchit la lumière d'excitation ayant des longueurs d'onde allant de 350 à 450 nanomètres.

6. Appareil selon l'une quelconque des revendications précédentes, dans lequel le filtre coloré de la source de lumière (310) est un filtre passe-bande interférentiel laissant passer une lumière d'excitation ayant des longueurs d'onde allant de 420 à 450 nanomètres.

7. Appareil selon l'une quelconque des revendications précédentes, comprenant en outre un filtre passe-bande (128) situé entre la lame séparatrice (120) et la première caméra (130), et arrangé de manière à laisser passer une lumière d'autofluorescence ayant des longueurs d'onde allant de 490 à 560 nanomètres.

8. Appareil selon l'une quelconque des revendications précédentes, comprenant en outre un filtre passe-haut rouge (124) situé entre la lame séparatrice (120) et la seconde caméra (126), le filtre passe-haut (124) ayant une limite de longueur d'onde de 630 nanomètres.

9. Appareil selon l'une quelconque des revendications précédentes, dans lequel le moniteur couleur (150) est un moniteur RVB ayant des prises d'entrée vidéo rouge, verte et bleue (150R, 150G, et 150B).

10. Appareil selon l'une quelconque des revendications précédentes, dans lequel la première (130) et seconde (126) caméras sont des caméras CDD à image intensifiée.

11. Appareil selon l'une quelconque des revendications précédentes, comprenant en outre une commande (202, 226) destinée à ajuster la fonction par laquelle le gain du premier ou du second signal d'image d'autofluorescence dépend du gain de l'autre du premier ou du second signal d'image d'autofluorescence.

12. Appareil selon l'une quelconque des revendications précédentes, dans lequel ladite source de lumière (100) est une source de lumière essentiellement monochrome.

13. Système de détection des tissus cancéreux ou pré-cancéreux comprenant l'appareil selon l'une quelconque des revendications précédentes et comprenant :

une source de lumière essentiellement monochrome (100) destinée à produire une lumière d'excitation (104) qui provoque l'émission par les tissus (110) sous examen d'une lumière d'autofluorescence ;

un endoscope (102) positionné de manière à recevoir la lumière d'excitation et à diriger la lumière d'excitation (104) dans une cavité interne du corps du patient et dans les tissus (110) sous examen ;

des moyens (114, 116) de collection de lumière d'autofluorescence (112) émise par les tissus (110) sous examen ;

ladite lame séparatrice (120) adaptée pour diviser la lumière d'autofluorescence recueillie en un premier faisceau ayant des longueurs d'onde telles qu'une intensité ( $R_{CIS}$ ) de la lumière d'autofluorescence des tissus anormaux est essentiellement différente de celle ( $R_N$ ) des tissus normaux et un second faisceau ayant des longueurs d'onde telles qu'une intensité ( $R_{CIS}$ ) de la lumière d'autofluorescence des tissus anormaux est es-

sentiellement la même que celle ( $R_n$ ) des tissus normaux ;  
une première (130) et seconde (126) caméra CDD à image intensifiée ou non- intensifiée destinée à recevoir  
le premier et second faisceaux de lumière d'autofluorescence respectivement, la première et seconde caméras  
CDD à image intensifiée ou non- intensifiée (130, 126) produisant un premier et un second signal d'image ; et  
5 ledit moniteur couleur (150) ayant une entrée de couleur rouge, bleue et verte, l'entrée de couleur rouge (150R)  
étant connectée de manière à recevoir l'un du premier ou du second signal d'image d'autofluorescence et les  
entrées de couleurs bleue et verte (150B, 150G) étant connectées de manière à recevoir l'autre du premier  
ou du second signal d'image d'autofluorescence pour produire une image sur écran ayant une couleur repré-  
sentative d'un taux d'amplitude du premier signal d'autofluorescence et du second signal d'autofluorescence,  
10 ladite image sur écran offrant un signe de normalité ou d'anormalité des tissus.

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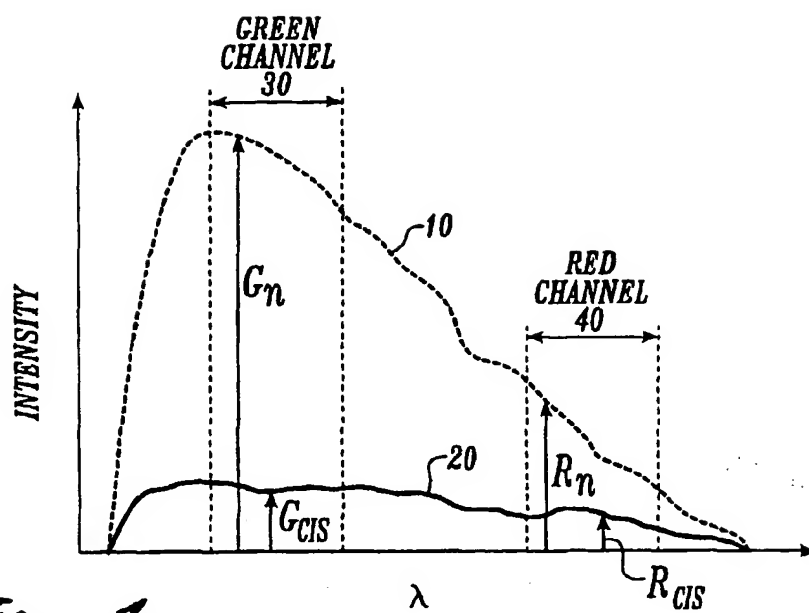


Fig. 1

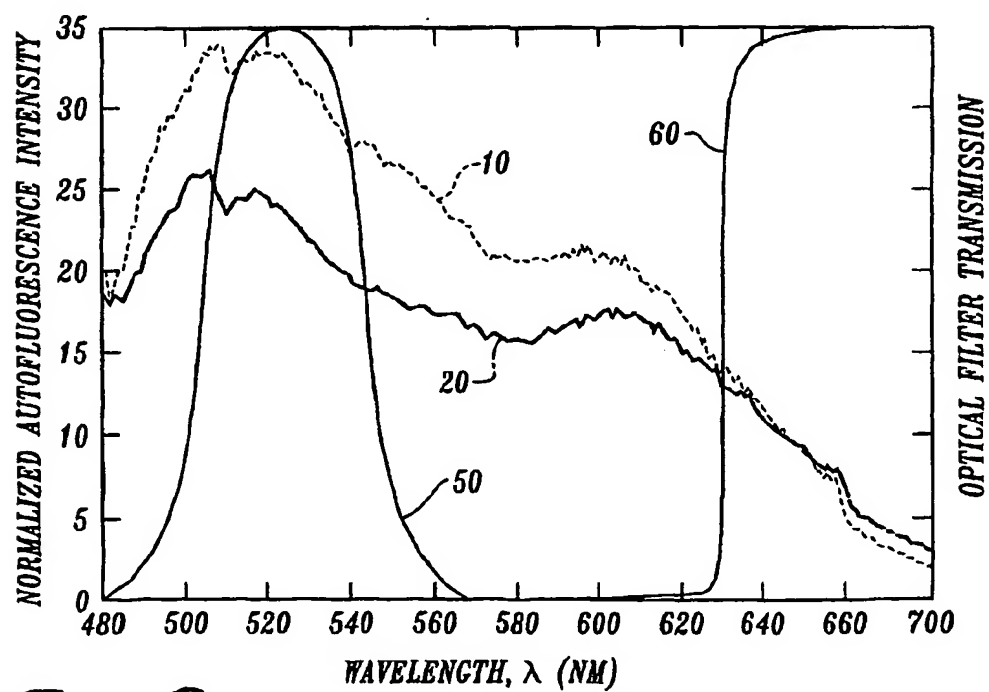
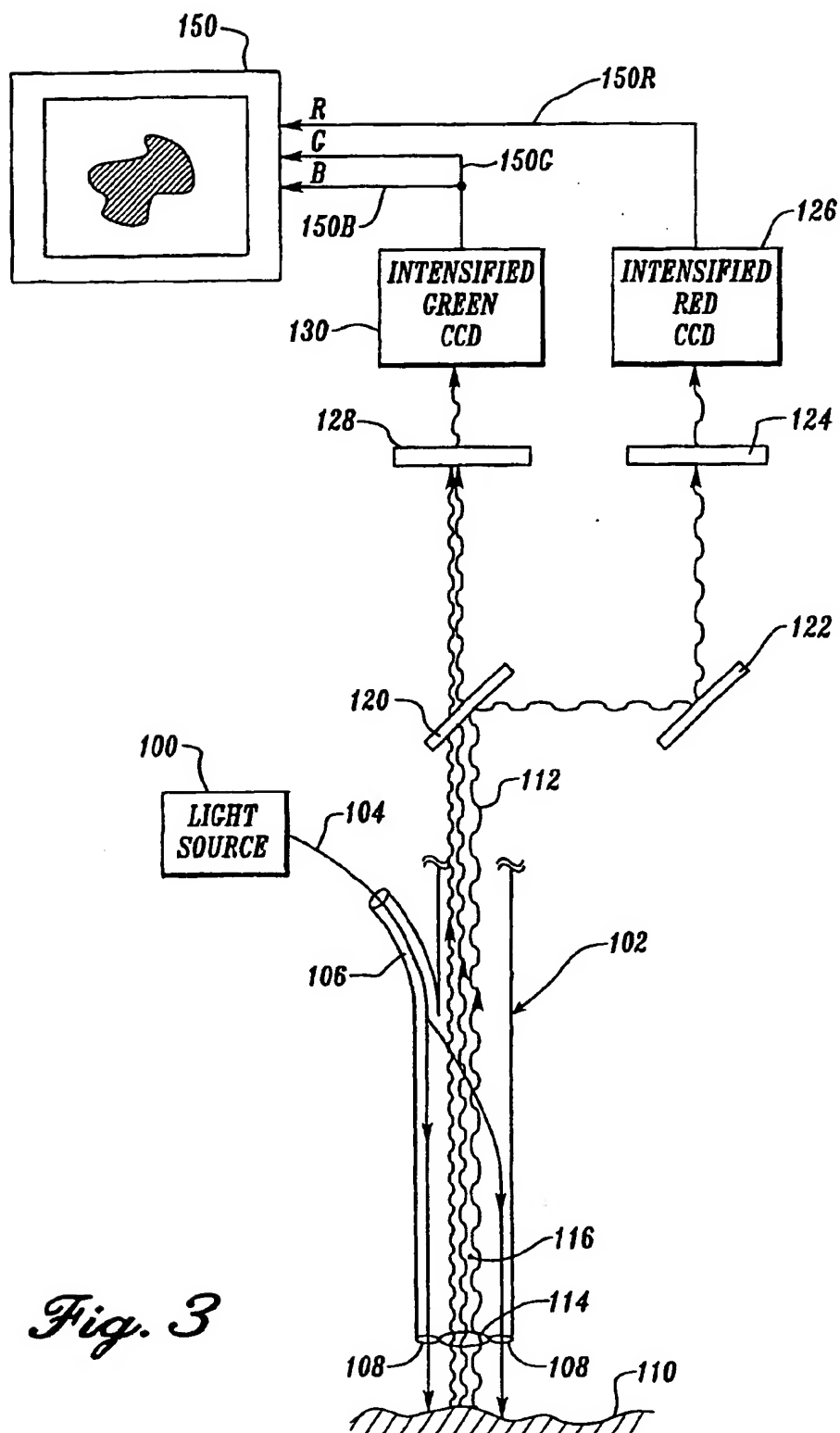


Fig. 2





*Fig. 3*

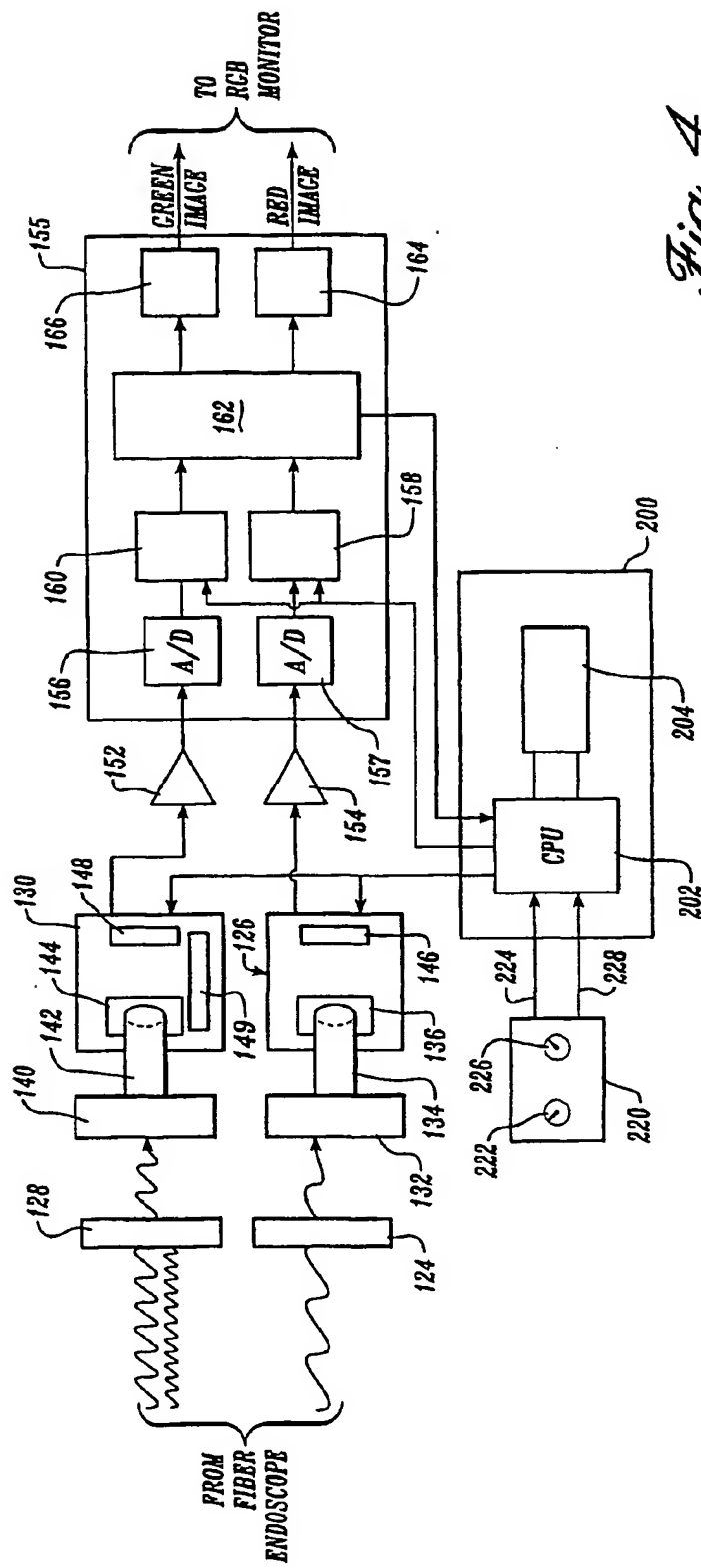
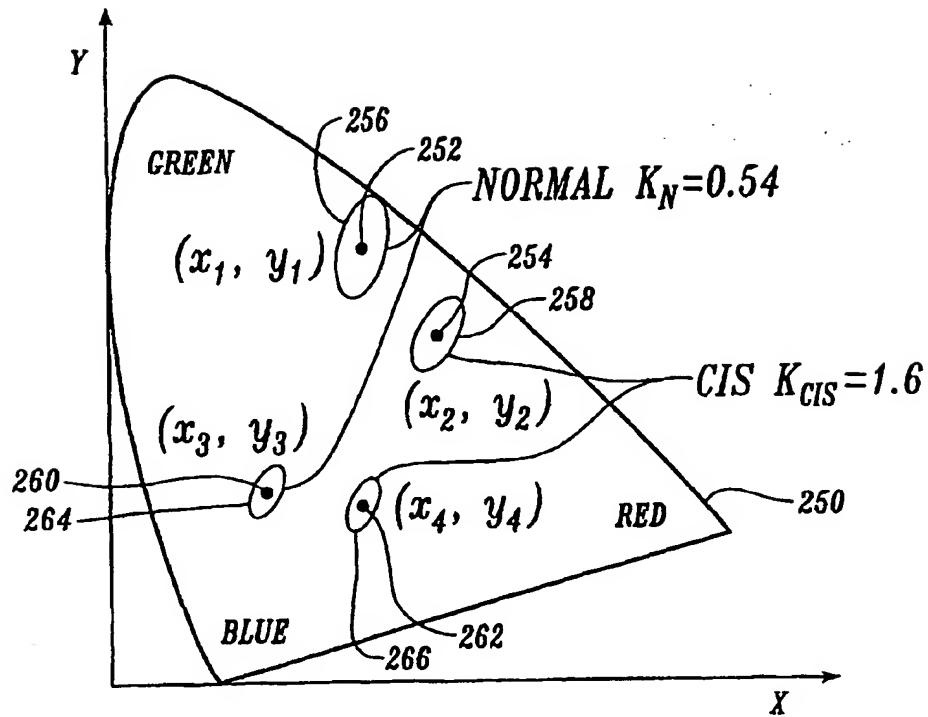


Fig. 4



*Fig. 5*

